PATENT COOPERATION TREATY

From the
INTERNATIONAL SEARCHING AUTHORITY

To:

see form PCT/ISA/220

PCT

WRITTEN OPINION OF THE INTERNATIONAL SEARCHING AUTHORITY

(PCT Rule 43*bis*.1)

Applicant's or agent's file reference see form PCT/ISA/220	Date of mailing *(day/month/year)* see form PCT/ISA/210 (second sheet) **FOR FURTHER ACTION** See paragraph 2 below

International application No.	International filing date *(day/month/year)*	Priority date *(day/month/year)*
PCT/GB2004/004621	01.11.2004	31.10.2003

International Patent Classification (IPC) or both national classification and IPC
G01N33/68

Applicant
PLASMACUTE AS

1. This opinion contains indications relating to the following items:

- ☒ Box No. I Basis of the opinion
- ☐ Box No. II Priority
- ☐ Box No. III Non-establishment of opinion with regard to novelty, inventive step and industrial applicability
- ☐ Box No. IV Lack of unity of invention
- ☒ Box No. V Reasoned statement under Rule 43*bis*.1(a)(i) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement
- ☐ Box No. VI Certain documents cited
- ☐ Box No. VII Certain defects in the international application
- ☐ Box No. VIII Certain observations on the international application

2. **FURTHER ACTION**

If a demand for international preliminary examination is made, this opinion will usually be considered to be a written opinion of the International Preliminary Examining Authority ("IPEA"). However, this does not apply where the applicant chooses an Authority other than this one to be the IPEA and the chosen IPEA has notifed the International Bureau under Rule 66.1*bis*(b) that written opinions of this International Searching Authority will not be so considered.

If this opinion is, as provided above, considered to be a written opinion of the IPEA, the applicant is invited to submit to the IPEA a written reply together, where appropriate, with amendments, before the expiration of three months from the date of mailing of Form PCT/ISA/220 or before the expiration of 22 months from the priority date, whichever expires later.

For further options, see Form PCT/ISA/220.

3. For further details, see notes to Form PCT/ISA/220.

Name and mailing address of the ISA:	Authorized Officer
European Patent Office D-80298 Munich Tel. +49 89 2399 - 0 Tx: 523656 epmu d Fax: +49 89 2399 - 4465	Thumb, W Telephone No. +49 89 2399-7350

Form (PCT/ISA/237) (Cover Sheet) (January 2004)

WRITTEN OPINION OF THE INTERNATIONAL SEARCHING AUTHORITY

International application No.
PCT/GB2004/004621

Box No. I Basis of the opinion

1. With regard to the **language**, this opinion has been established on the basis of the international application in the language in which it was filed, unless otherwise indicated under this item.

   ☐ This opinion has been established on the basis of a translation from the original language into the following language , which is the language of a translation furnished for the purposes of international search (under Rules 12.3 and 23.1(b)).

2. With regard to any **nucleotide and/or amino acid sequence** disclosed in the international application and necessary to the claimed invention, this opinion has been established on the basis of:

   a. type of material:

   ☐ a sequence listing

   ☐ table(s) related to the sequence listing

   b. format of material:

   ☐ in written format

   ☐ in computer readable form

   c. time of filing/furnishing:

   ☐ contained in the international application as filed.

   ☐ filed together with the international application in computer readable form.

   ☐ furnished subsequently to this Authority for the purposes of search.

3. ☐ In addition, in the case that more than one version or copy of a sequence listing and/or table relating thereto has been filed or furnished, the required statements that the information in the subsequent or additional copies is identical to that in the application as filed or does not go beyond the application as filed, as appropriate, were furnished.

4. Additional comments:

WRITTEN OPINION OF THE INTERNATIONAL SEARCHING AUTHORITY

International application No.
PCT/GB2004/004621

Box No. V Reasoned statement under Rule 43*bis*.1(a)(i) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement

1. Statement

Novelty (N)	Yes:	Claims	7-10
	No:	Claims	1-6,11-39
Inventive step (IS)	Yes:	Claims	
	No:	Claims	1-39
Industrial applicability (IA)	Yes:	Claims	1-39
	No:	Claims	

2. Citations and explanations

see separate sheet

Re Item V

Reasoned statement with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement

1. Document WO-96/26443 (D1) is novelty-destroying for the subject-matter of claims 1, 3-6, 11-17, 19-29, 33-35, and 39 (Article 33(2) PCT).
D1 discloses methods for detection of antibody production in a blood sample. The method comprises the steps of incubating lymphocytes from the blood sample with an appropriate solid surface in order to immobilise antibodies to be detected, removing the cells and detecting antibodies bound to the solid surface. Small samples volumes below 1 ml can be used. Antibody production is detected without a prior step of pre-culturing the lymphocytes. Erythrocytes present in the sample may be lysed prior to the analysis. Useful lymphocyte or leukocyte populations can be separated. The blood sample may also be used directly. Additional and useful data on pre-existing serum/plasma antibodies can be obtained in a classical ELISA test. After separation of lymphocytes from the blood sample the remaining plasma fluid may be used for detecting pre-existing antibodies using the same binding partner-coated solid phase used in the assay of the invention (see the passages cited in the international search report).
It should be pointed out that even though a number of differences to existing methods, e.g. to those disclosed in document D1, and advantages resulting therefrom are listed in the specification of the present application, these differences are not reflected in the wording of claim 1.
For example, claim 1 does not specify the conditions under which the assays are performed, for example whether cell culturing is used or not, or how the sample is treated.
Moreover, from the passage on page 10, lines 12-24, it appears that the term "lymphocyte antibodies" also includes antibodies which are produced by the lymphocytes after the sample has been taken, as disclosed in document D1.
Therefore, D1 is novelty-destroying for the subject-matter of claims 1, 3-6, 11-17, 19-29, 33-35, and 39 within the meaning of Article 33(2) PCT.

2. Document WO-00/77525 (D2) is novelty-destroying for the subject-matter of claims 1-6 and 11-39 in the sense of Article 33(2) PCT.
D2 discloses a method for determining the presence or amount of antibodies synthesised in lymphocytes. The sample may be a blood sample (page 7,

paragraph 2) and the assay can be performed on samples which have been stored refrigerated (paragraph bridging pages 4 and 5). After separation of the lymphocytes they are disrupted (page 8, 1st full paragraph). Small sample volumes can be used (page 17, paragraph 1). The antibodies are detected using e.g. ELISA assays. The information obtained from the assay can be supplemented by using other assay methods. Additional and useful data on pre-existing serum/plasma antibodies can be obtained in a classical ELISA test. After separation of the lymphocytes the remaining plasma fluid may be used for detecting said pre-existing antibodies (page 23, lines 26-38).

3. Claims 7-10 do not appear to be inventive within the meaning of Article 33(3) PCT in view of the teaching of documents D1 and D2. Combining the samples containing serum antibodies and antibodies derived from disrupted lymphocytes in one sample would appear to be obvious in view of the explicit reference in documents D1 and D2 to the additional use of plasma samples for obtaining additional information on antibodies present in a blood sample, taking into consideration that said combining of the samples does not appear to result in a surprising technical effect apart from the obvious simplification of the assay.